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EXAMINER	
RIGGS II, LARRY D	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,759	PALECEK ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 08 September 2004 and 04 May 2005 are acknowledged and entered.

Status of Claims

Cancellation of claims 1-34 are acknowledged. Claims 34-77 are currently pending and under consideration.

Specification

The abstract of the disclosure is objected to because of undue length. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-39, 42, 43, 45, 47-53, 55-57, 61-68, 73 and 74 provide various numbers in parenthesis throughout the above claims, e.g. analyte (10), probe (20), probe (22), site (12), in lines 1, 3, 5, 9, 10 and 12 of claim 34. The metes and bounds of said numbers are unclear.

Claim 34 recites the limitation, "labeling the first and second probes with a first and a second electro-chemical label, respectively, if the first and second probes are not already electro-chemically reactive" in lines 6-7. The metes and bounds of the limitation are unclear. It is unclear as to what is meant by "a probe is electro-chemically active." Does that mean that a probe must be labeled with an electro-chemical label to be electro-chemically active or may a probe be inherently electro-chemically active without said label, or may a probe be labeled with something other than an electro-chemical label to be electro-chemically active?

Claim 34 recites the limitation "abstracting the first and second probes bound to the analyte" in line 8. The metes and bounds of the limitation are unclear. The specification provides a non-limiting definition of abstracting as "separation of the bound from the unbound first or second probes or of the bound from the unbound analyte." (page 9, lines 27-29). One skilled in the art would be unclear of the meaning of the limitation because the wording of the limitation seems to indicate that it is possible for analyte bound to a first probe or analyte bound to a second probe, i.e. the complex of

the first probe and the analyte only or the complex of the second probe and the analyte only, may be abstracted from other components in the fluid.

Claim 35 recites the limitation, "labeling the first probe and the analyte with a first electro-chemical label and an analyte electro-chemical label, respectively, if the first probe and analyte are not already electro-chemically reactive" in lines 6-7. The metes and bounds of the limitation are unclear. It is unclear how one skilled in the art determines whether a probe and analyte are electro-chemically active? Does that mean that a probe and analyte must be labeled with an electro-chemical label to be electro-chemically active or may a probe and analyte be inherently electro-chemically active without said label, or may a probe and analyte be labeled with something other than an electro-chemical label to be electro-chemically active?

Claim 35 recites the limitation "abstracting the analyte bound by the first probe and the first probe bound to the analyte" in line 9. The metes and bounds of the limitation are unclear. The specification provides a non-limiting definition of abstracting as "separation of the bound from the unbound first or second probes or of the bound from the unbound analyte." (page 9, lines 27-29). One skilled in the art would be unclear of the meaning of the limitation because the wording of the limitation seems to indicate that only analyte bound to a first probe, i.e. the complex of the first probe and the analyte, is being abstracted from the rest in the fluid.

Claim 36 recites the limitation "the detection" in line 2. There is no clear antecedent basis for the limitation. Claim 34 provides for the detection of a first electro-

chemical signal and a second electro-chemical signal, whereas claim 35 provides for the detection of a first electro-chemical signal and an analyte electro-chemical signal.

Claim 48 recites the limitation "the analyte is amplified by PCR prior to step a), in lines 1-2. There is no clear antecedent basis for the limitation. Neither claim 34 or 35 have a "step a)".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 55, 67, 68, 70, 71, 74, 76 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem., 1997, 69, 3915-3920) and further in view of Xu et al. (Analyst, 2000, 126, 62-65).

The instant claim 34 provides a method for characterizing an analyte contained in a first fluid, comprising the steps of:

contacting the analyte with a first probe and a second probe under conditions in which the first and second probe bind to the analyte, wherein the first probe binds specifically to at least one first binding site of the analyte;

labeling the first and second probes with a first and a second electro-chemical label, respectively, if the first and second probes are not already electro-chemically reactive;

abstracting the first and second probes bound to the analyte;

detecting a first electro-chemical signal (Si 1) caused by the first-labeled probe and a second electro-chemical signal (Si 2) caused by the second-labeled probe; and

determining the ratio between the first (Si 1) and the second signal (Si 2), thereby characterizing the analyte.

Regarding claim 34, Kamihara et al. shows a fluorescently labeled probe and a fluorescently active intercalator (ethidium homodimer), labeling an analyte (DNA) with said fluorescently labeled probe and said fluorescently labeled intercalator, separating

unbound probe and intercalator from bound, detecting signals from both the fluorescently labeled probe and said fluorescently labeled intercalator and from the ratio of the signals or the probe and intercalator, characterizing the identity and length of the DNA, (see paragraphs [0008], [0019], [0032]).

Kamihara et al. does not show contacting electrochemically labeled first and second probes to an analyte.

Castro et al. shows contacting analyte to a first probe and second probe via their specific complimentary sequences, (see page 3916, left column, first full paragraph; Figure 1).

Kamihara et al. and Castro et al. do not show electrochemically labeled probes.

Xu et al. shows electrochemically active ferrocene-oligonucleotides that allow electrochemical detection of DNA by hybridizing to a single strand of DNA through a specific sequence and detected with voltammetry, (see abstract, page 64, left column, paragraphs 1 and 2; Figures 1-4).

Regarding claim 55, Castro et al. shows a second probe binding specifically to at least one second binding site, (see Figure 1).

Regarding claims 67 and 68, Kamihara et al. shows a first oligonucleotide probe hybridizing to DNA analyte via a specific sequence, (see paragraph [0040-41], Figure 2]).

Regarding claim 74, Kamihara et al. shows a linear oligonucleotide probe with an end label, (see figure 2).

Regarding claims 70-71 and 76-77, Xu et al. shows electrochemical detection by cyclic voltammetery, wherein the aminoferrocene is reversibly reduced and oxidized, (see page 63, right column, paragraphs 3-4).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al. and the electrochemically active probes by Xu et al. because the method of Castro et al. enables simple and reliable sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph) and the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph).

Claims 35-45, 47-49 and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem.,1997, 69, 3915-3920) in view of Xu et al. (Analyst, 2000, 126, 62-65) and further in view of Mishima et al. (Anal. Chim. Acta, 1997, 345, 45-50).

The instant claim 35 provides a method for characterizing an analyte contained in a first fluid, comprising the steps of:

contacting an analyte with a first probe under conditions in which the first probe binds to the analyte, wherein the first probe binds specifically to at least one first binding site of the analyte;

labeling the first probe and the analyte with a first electro-chemical label and an analyte electro-chemical label, respectively, if the first probe and analyte are not already electro-chemically reactive;

abstracting the analyte bound by the first probe and the first probe bound to the analyte;

detecting a first electro-chemical signal (Si 1) caused by the first-labeled probe and an analyte electro-chemical signal (Si A) caused by the labeled analyte; and

determining the ratio between the first (Si 1) and the analyte signal (Si A), thereby characterizing the analyte.

Regarding claim 35, Kamihara et al. shows a fluorescently labeled probe and a fluorescently active intercalator (ethidium homodimer), labeling an analyte (DNA) with said fluorescently labeled probe and said fluorescently labeled intercalator, separating unbound probe and intercalator from bound, detecting signals from both the fluorescently labeled probe and said fluorescently labeled intercalator and from the ratio of the signals or the probe and intercalator, characterizing the identity and length of the DNA, (see paragraphs [0008], [0019], [0032]).

Kamihara et al. does not show contacting electrochemically labeled first probe to an analyte and electrochemically labeling analyte.

Castro et al. shows contacting analyte to a first probe via a specific complimentary sequence, (see page 3916, left column, first full paragraph; Figure 1).

Kamihara et al. and Castro et al. do not show electrochemically labeled probes or electrochemically labeling analyte.

Xu et al. shows electrochemically active ferrocene-oligonucleotides that allow electrochemical detection of DNA by hybridizing to a single strand of DNA through a specific sequence and detected with voltammetry, (see abstract, page 64, left column, paragraphs 1 and 2; Figures 1-4).

Kamihara et al., Castro et al. and Xu et al. do not show electrochemically labeling analyte.

Mishima et al. shows a method of binding Tris(bipyridyl)osmium(II/III) ion (osmium complex) within the major and minor grooves of double stranded DNA that allow the resulting DNA-osmium complex to be detected by voltammetry, (see page 46, paragraph 2.5; page 48, paragraphs 3.2-3.3; page 50, paragraph 4).

Regarding claim 36, Kamihara et al. shows the removal of the unbound probes in solution by filtration before detection, (see paragraph [0032]).

Kamihara et al. does not show detection with an electrode.

Xu et al. shows voltammetry conducted with an electrode in solution, (see page 63, left column).

Regarding claim 37, Kamihara et al. shows removal unbound probe and intercalator of a first solution with a spin filter and detection in a second solution, (see [0032]).

Regarding claims 38-40, Xu et al. shows analyte bound to a catcher molecule with is immobilized on a first surface, wherein the catcher molecule is an analogue of a nucleic acid, (see page 63, left column, last paragraph – right column, third paragraph; Figures 1 and 2).

Regarding claims 41-45, Kamihara et al. shows biotin at one end of the probe that hybridizes to the analyte, wherein the analyte is DNA, (see paragraph [0033]).

Regarding claim 47, Kamihara et al. shows determining the length of DNA, (see paragraph [0008]).

Regarding claim 48, Kamihara et al. shows target DNA amplified by PCR, (see paragraphs [0024-25]).

Regarding claim 49, Kamihara et al. shows analyte (DNA) immobilized on a first surface, (see paragraph [0026]).

Regarding claims 61-66, Kamihara et al. shows the enzymatic digestion and release of the first probe from the analyte and second probe prior to detection, (see paragraph [0042]).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al. and the electrochemically active probes by Xu et al. because the method of Castro et al. enables simple and reliable sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph), the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph) and the binding of osmium complexes along the DNA backbone by Mishima et al. provides an electrochemical active probes throughout the length of the DNA, (see page 48, paragraph 3.3).

Claims 46 and 71-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem.,1997, 69, 3915-3920) in view of Xu et al. (Analyst, 2000, 126, 62-65) in view of Mishima et al. (Anal. Chim. Acta, 1997, 345, 45-50) as applied to claim 35 above, and further in view of Bamdad et al. (US Pat. Pub. 2003/0087228).

The instant claims 46 and 71-75 are drawn to a method for characterizing an analyte contained in a first fluid, comprising the steps of: contacting an analyte with a first probe or first and second probes under conditions in which the probe(s) binds to the analyte, wherein the probe(s) bind specifically to at least one first binding site of the analyte; labeling the probe(s) or additionally the analyte, with electro-chemical label(s) and an analyte electro-chemical label, respectively, if the probe(s) and analyte are not already electro-chemically reactive; abstracting bound probe(s); detecting a electro-chemical signal(s) (Si 1)/(Si 2) and an analyte electro-chemical signal (Si A); and determining the ratio between the first (Si 1) and the analyte signal (Si A)/second signal (Si 2), thereby characterizing the analyte, wherein the analyte is a nucleic acid that has a poly T end or a poly A end, wherein the labels are dyes from a possible group of dyes, probes are multiple labeled, or linear and labeled at one end, and detection takes place on the same electrode.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. are applied to claim 35 above.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. do not show nucleic analyte with a poly T end or a poly A end.

Regarding claim 46, Bamdad et al. shows a method of selecting mRNA containing a poly A tail by a poly T probe, (see paragraph [0383]).

Regarding claim 71-75 Bamdad et al. shows probes may contain labels from dyes, such as xanthene dyes and azine dyes, (see paragraphs, [0015], [0166]), Bamdad et al. shows a linear probe, wherein one end may be labeled with a multiple electron transfer moieties (ETM), (see paragraph [0012], [0222]), multiple (ETMs) may be placed on a probe, (see paragraphs [0012-0015], [0037], [0169-0170], [0222]) and detection of signals from two different probes on the same electrode, (see paragraphs [0033-34], [0163], [0199]).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al., the electrochemically active probes by Xu et al. and the arrays and probes by Bamdad et al. because the method of Castro et al. enables simple and reliable sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph), the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph) and the binding of osmium complexes along the DNA backbone by Mishima et al. provides an electrochemical active probes throughout the length of the DNA, (see page 48, paragraph 3.3) and the electrochemically active poly-T probes that capture poly-A tailed mRNA and other ETM labeled probes, decreases the amount of different probe synthesis that is done and for

various purposes such as calibration or internal standards, (see paragraphs [0199] and [0383].

Claims 49-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem.,1997, 69, 3915-3920) in view of Xu et al. (Analyst, 2000, 126, 62-65) in view of Mishima et al. (Anal. Chim. Acta, 1997, 345, 45-50) as applied to claim 35 above, and further in view of Leland et al. (6,078,782, issued June 20, 2000).

The instant claims 49-54 are drawn to a method for characterizing an analyte contained in a first fluid, comprising the steps of: contacting an analyte with a first probe or first and second probes under conditions in which the probe(s) binds to the analyte, wherein the probe(s) bind specifically to at least one first binding site of the analyte; labeling the probe(s) or additionally the analyte, with electro-chemical label(s) and an analyte electro-chemical label, respectively, if the probe(s) and analyte are not already electro-chemically reactive; abstracting bound probe(s); detecting a electro-chemical signal(s) (Si 1)/(Si 2) and an analyte electro-chemical signal (Si A); and determining the ratio between the first (Si 1) and the analyte signal (Si A)/second signal (Si 2), thereby characterizing the analyte, wherein the analyte is bound to a first/second surface, wherein the suface is a 1-100 micrometer superparamagnetic particle, and the second surface is an electrode of possible various metals.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. are applied to claim 35 above.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. do not show analyte bound to a first or second surface, a 1-100 micrometer superparamagnetic particle, and the second surface as an electrode of possible various metals.

Regarding claims 49-54, Leland et al. disclose methods of a binding assay for an analyte of interest present in a sample based on electrochemiluminescence at an electrode of interest. (See the Abstract). The method applies first surface microparticles which are magnetic beads (See column 17, lines 8) and a probe which is streptavidin beads having specific affinity for the PCR product labeled with biotin and an ECL label (See column 18, lines 22-26). The beads bound PCR product was washed (See column 18, lines 26) then subject to analysis detecting the label (See column 18, lines 27-28). This teaching is inherent that the first microparticles are transferred into a second solution for detecting the nucleic acid in such manner that the electrode is used for the electrochemical detection. The particle sizes can range from 0.001 to 100 micrometers and preferable from 0.01 to 10 micrometers, (see column 18, lines 2-3). The ECL moieties are metal chelates in which the metal is osmium (See column 10, lines 29-35). Microparticles are parallel and perpendicular to the second surface of the working electrode, in vicinity of the surface under magnetic field (See column 21, lines 52-57). The electrode comprises gold (See column 16, lines 14-18).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al., the electrochemically active probes by Xu et al. and the paramagnetic bead assay by

Leland et al. because the method of Castro et al. enables simple and reliable sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph), the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph) and the binding of osmium complexes along the DNA backbone by Mishima et al. provides an electrochemical active probes throughout the length of the DNA, (see page 48, paragraph 3.3) and the bead assay would provide a precise, sensitive and fast reproducible assay, (see column 5, lines 6-9).

Claims 56-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem., 1997, 69, 3915-3920) in view of Xu et al. (Analyst, 2000, 126, 62-65) as applied to claim 34 and 55 above, further in view of Kremer et al. (Science, 1991, 252, 1711-1714).

The instant claims 56-60 provide a method for characterizing an analyte contained in a first fluid, comprising the steps of: contacting the analyte with a first probe and a second probe under conditions in which the first and second probe bind to the analyte, wherein the first probe binds specifically to at least one first binding site of the analyte; labeling the first and second probes with a first and a second electro-chemical label, respectively, if the first and second probes are not already electro-chemically reactive; abstracting the first and second probes bound to the analyte; detecting a first electro-chemical signal (Si 1) caused by the first-labeled probe and a second electro-chemical signal (Si 2) caused by the second-labeled probe; and determining the ratio

between the first (Si 1) and the second signal (Si 2), thereby characterizing the analyte, wherein the analyte has a known number of first binding sites and unknown number of second binding sites, the second probe binds to repetitive sequences and the first probe does not, wherein the repetitive sequences are a consequence of a triplet expansion disease from a potential list of diseases.

Kamihara et al., Castro et al. and Xu et al. are applied to claim 34 and 55 above.

Kamihara et al., Castro et al. and Xu et al. do not show the analyte having a known number of first binding sites and unknown number of second binding sites, the second probe binding to repetitive sequences and the first probe not, wherein the repetitive sequences are a consequence of a triplet expansion disease from a potential list of diseases.

Regarding claims 56-60, Kremer et al. shows DNA fragments the exhibit repetitive (CCG)n sequences that are a consequence of the triplet expansion disease, fragile X Syndrome and probes that bind to the repetitive sequence and probes that do not bind to the repetitive sequence, wherein the number of repetitive sequence binding sites were unknown, (see page 1711, first paragraph; 1713, left column, last paragraph – middle column, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al., the electrochemically active probes by Xu et al and the method of probes that hybridize repetitive sequences, because the method of Castro et al. enables simple and reliable

sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph), the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph) and the repetitive sequence hybridizing probes would enable analysis of samples that may indicate repetitive sequences that are linked to triplet expansion diseases, (see page 1711, first paragraph).

Claim 69 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kamihara et al. (JP 11-164700) in view of Castro et al. (Anal. Chem.,1997, 69, 3915-3920) in view of Xu et al. (Analyst, 2000, 126, 62-65) in view of Mishima et al. (Anal. Chim. Acta, 1997, 345, 45-50) as applied to claim 35 above, and further in view of Pershad et al. (Biochemistry, 1999, 38, 8992-8999).

The instant claim 69 is drawn to a method for characterizing an analyte contained in a first fluid, comprising the steps of: contacting an analyte with a first probe or first and second probes under conditions in which the probe(s) binds to the analyte, wherein the probe(s) bind specifically to at least one first binding site of the analyte; labeling the probe(s) or additionally the analyte, with electro-chemical label(s) and an analyte electro-chemical label, respectively, if the probe(s) and analyte are not already electro-chemically reactive; abstracting bound probe(s); detecting a electro-chemical signal(s) (Si 1)/(Si 2) and an analyte electro-chemical signal (Si A); and determining the ratio between the first (Si 1) and the analyte signal (Si A)/second signal (Si 2), thereby

characterizing the analyte, wherein the first signal (Si 1), second signal (Si 2) or analyte signal (Si A), is caused by a catalytic hydrogen release.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. are applied to claim 35 above.

Kamihara et al., Castro et al., Xu et al. and Mishima et al. do not show first signal (Si 1), second signal (Si 2) or analyte signal (Si A), is caused by a catalytic hydrogen release.

Regarding claim 69, Pershad et al. shows a method of monitoring of Cv hydrogenase by protein film voltammetry, wherein signals are detected from the oxidation and production of hydrogen, (see abstract, page 8993, left column, paragraphs 1-2; Figures 1-2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of DNA detection and analysis by Kamihara et al. with the method of using two sequence specific probes by Castro et al., the electrochemically active probes by Xu et al. and the voltammetry methods by Pershad et al. because the method of Castro et al. enables simple and reliable sensitive detection of specific nucleic acid sequences, (see page 3920, right column, second paragraph), the use of electrochemically active probes by Xu et al. have the advantage of being cheap, sensitive and rapid, (see page 62, first paragraph) and the binding of osmium complexes along the DNA backbone by Mishima et al. provides an electrochemical active probes throughout the length of the DNA, (see page 48, paragraph 3.3) and the detection of signals by hydrogen oxidation and production by

Pershad et al. allows measurements of very high catalytic rates of hydrogenase, (see page 8998, last paragraph – 8999, first paragraph).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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